REMARKS

Interview

Applicant would like to thank the Examiner for the interview conducted on 12/3/03. The Examiner summarized the interview by noting that Applicant had " [p]resented exhibits to support effective filing date for Gentz 03/03/00 case instead of 1/13/98. If Gentz does not receive benefit of priority to 1998 for purposes of 35 U.S.C. 102 rejection, rejection should be withdrawn as Gentz is not available as prior art." Applicant notes that the "exhibits" referred to in the Interview Summary were the figure showing the family tree of the '583 publication set forth on page 4, *infra,* a copy of the '583 publication, and copies of the '352 and '496 applications.

Priority

Applicant notes that the Examiner has made certain observations regarding the support for the present claims in one or more earlier-filed applications to which Applicant has claimed priority. Those observations lead the Examiner to assert that the present claims are not entitled to a filing date prior to July 30, 1998. *See* 8/4/03 Office Action at page 2. Applicant does not agree with the Examiner's assertion regarding the effective filing date of the present claims, and expressly reserves the right to dispute such assertion if necessary at a later time. Applicant also believes that the response provided herein fully addresses the outstanding rejections in a manner that does not require resolution of the question of priority of Applicant's pending claims.

Rejection of claims 67-77 and 79-84 under 35 U.S.C. § 102(e) in view of Gentz et al. (US 2002/0150583 A1) (hereinafter the '583 publication")

The Examiner asserts that the '583 publication teaches a TNFR-6α polypeptide (SEQ ID NO:2) that has a sequence identical to the DcR3 polypeptide (SEQ ID NO:1) of the instant application. In addition, the Examiner asserts that the '583 publication teaches antibodies that bind and are agonistic or antagonistic anti-TNFR-6α antibodies, including fragments, monoclonals, polyclonals, recombinant, chimeric and human antibodies, as well as methods of making such antibodies and expressing them, and antibody-producing host cells. Finally, the Examiner asserts that the '583 publication shows that TNFR-6α binds to FasL in Figures 7A-B and that antagonistic antibodies include those that block the binding of TNFR-6α with not only

Fas ligand, but also inherently LIGHT. Applicant respectfully traverses the rejection for at least the following reasons.

Applicant notes that it is well-settled law that a patent (and, by implication, a patent application published pursuant to 35 U.S.C. 122(b)) shall have effect under 35 U.S.C. § 102(e) as of a particular date only to the extent that there is a sufficient disclosure under 35 U.S.C. § 112, first paragraph, for the subject matter in question. If the patent or published application claims the benefit under 35 U.S.C. §120 (and by implication under 35 U.S.C. §119(e)) to an earlier filed application, that patent or published application shall not be entitled to prior art effect under §102(e) if the earlier filed application does not provide a sufficient disclosure under 35 U.S.C. §112, first paragraph, for the subject matter in question. To be given effect under § 102(e), the claims of the reference patent must be supported in the manner required by 35 U.S.C. § 112 in the priority application whose date is relied on to establish the prior art status of the patent. *See In re Wertheim*, 646 F2d 527, 209 USPQ 554 (CCPA 1981); and MPEP 2136.03, sub-heading IV.

The '583 publication claims priority to two applications filed prior to July 30, 1998, the priority filing date the Examiner asserts for the instant application. Those two applications are U.S.S.N. 09/006,352, filed January 13, 1998 ('352 application) and U.S. provisional application No. 60/035,496, filed January 14, 1997 ('496 application). A complete "family tree" for the '583 publication relative to the July 30, 1998 priority filing date of the current application is provided below for the Examiner's convenience. It is important to note that the Examiner has afforded the '583 publication an effective filing date of January 13, 1998 based on the filing of the '352 application, but refused to give the '583 publication a § 102(e) effective date based on the '496 application. *See* 8/4/03 Office Action at page 2. The Examiner did not provide any reasoning for these conclusions, and Applicant disagrees that the '583 publication should be afforded the effective filing date of the '352 application. As set forth below, the '352 application fails to provide an adequate written description or enabling disclosure for isolated antibodies, including agonist or antagonist antibodies, to the DcR3 receptor sufficient to satisfy the requirements of § 112. Consequently, the '583 publication is not entitled to a prior art effect as of the filing date of the '352 application and, as such, is not prior art to the present claims.

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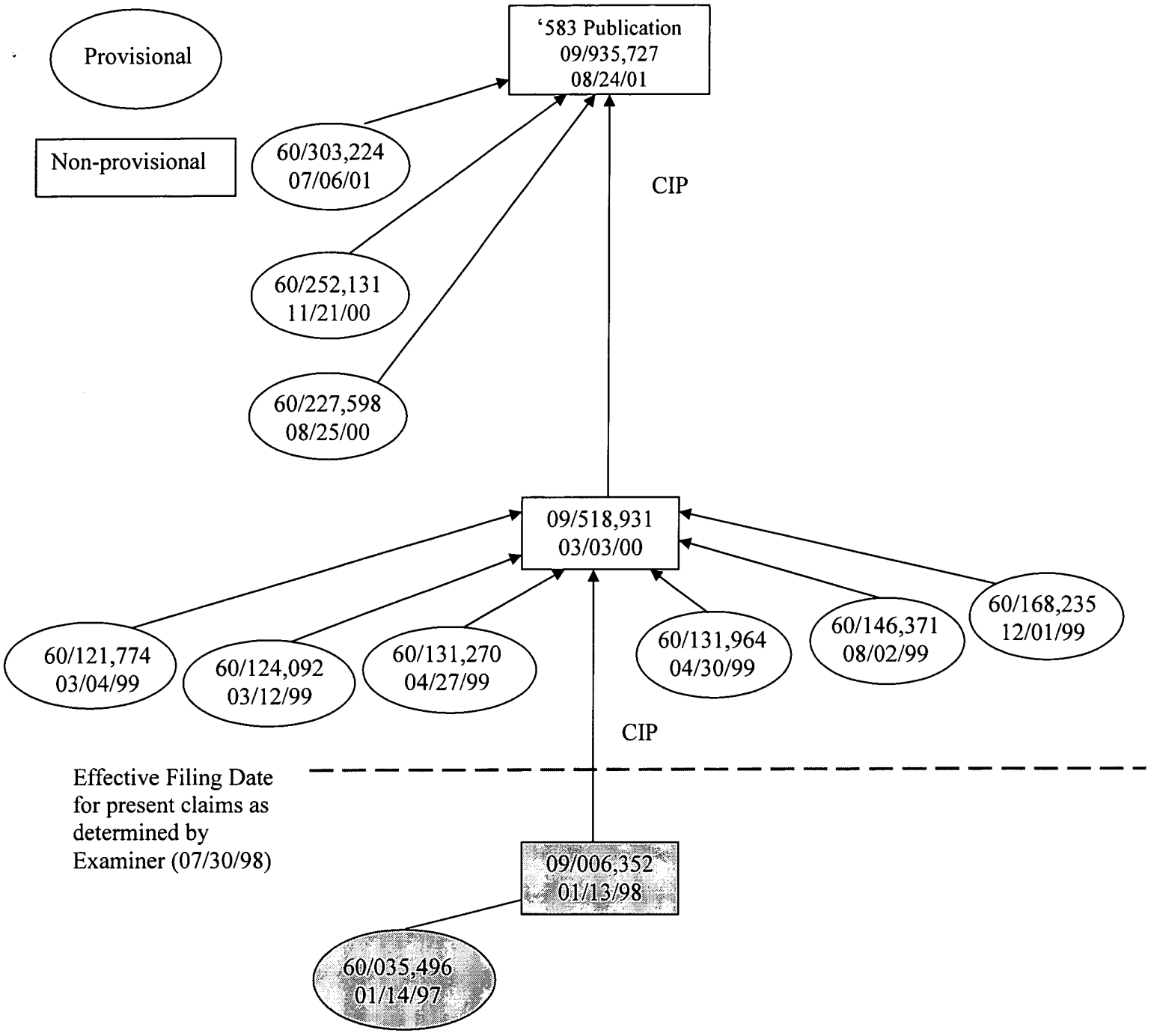
'583 Publication Family Tree



Applicant notes in particular that certain information regarding TNFR-5 that is included in the first-filed application (i.e., the '496 application) has been deleted from and is not present in the later-filed '352 application. Applicant further notes that the disclosures of the '352 and '496 applications with respect to TNFR-6α are almost identical. Indeed, upon comparing the relevant disclosure of the two applications, Applicant was not able to discern any additional disclosure in the '352 application (relative to the '496 application) that would justify the Examiner's conclusion that the '352 and '496 applications should be treated differently relative to the support they do or do not provide for the '583 publication under § 102(e). For instance, neither the '352 nor the '496 applications contain any experimental data characterizing the activity or function of TNFR-6α, and neither application identifies a ligand(s) of TNFR-6α. As a matter of fact, the ligands to which TNFR-6α binds, AIM-II and FasL, were first disclosed by the applicant of the '583 publication in its 60/121,774 provisional application ("the '774 application"). See, e.g., p. 17, lines 8-10 and Example 7 of the '774 application. Such disclosures regarding the ligands of TNFR-6α are not present in the '352 or '496 applications. Applicant notes that the '774 application was filed after the effective filing date recognized by the Examiner for the current claims.

Applicant also notes that most of the passages of the '583 publication relied upon by the Examiner in rejecting the pending claims (*See* 8/4/03 Office Action, p. 3) are *not* found in the '352 or '496 applications. For example, Figures 7A-B of the '583 application—and the experiments upon which those figures are based—are not present in the '352 application. Accordingly (and as discussed above), contrary to the Examiner's assertion, the '352 application does not identify the ligands bound by TNFR-6α. The Examiner also cited sections [0371] and [0396] of the '583 publication as disclosing that "TNFR-6α *antagonists*, which necessarily include antibodies, are those that *inhibit growth of cancers*....[emphasis added]" The '352 application, however, discloses just the opposite. The '352 application teaches that one method for enhancing apoptosis—and thereby inhibiting cancer—is to administer to a cell a TNFR *agonist* capable of increasing TNFR mediated signaling. *See, e.g.,* p. 39, lines 36 – p. 40, line 8. The applicant of the '352 application apparently recognized the error it had made regarding the predicted functional effect of binding to the receptor and altered the disclosure of subsequent filings (e.g., the '583 publication) to reflect the functions actually triggered by binding to the receptor. *See, e.g.,* p. 57, section [0396] of the '583 publication.

Finally, Applicant notes that while the specification of the '352 application postulates that it may be possible to produce antagonistic and agonist antibodies that bind to TNFR-6α (*See, e.g.,* p. 41, line 36 – p. 42, line 22), such disclosure fails to satisfy the requirements of § 112, first

paragraph, for the currently claimed subject matter. Recognizing the unpredictable nature of this field, without any teaching of a function or activity of the receptor or the identity of a ligand that binds the putative receptor, the disclosure of the '352 application cannot provide an adequate written description for an antibody meeting the requirements of the pending claims, and certainly does not enable one of ordinary skill to produce such an antibody.

Applicant also notes that the '352 application contains various disclosures that tend to refute the Examiner's assertion the '583 publication is entitled to the '352 application's January 13, 1998 filing date. In particular, Applicant directs the Examiner's attention to the following points disclosed in the '352 application:

- The '352 application discloses that TNFR-6α was expressed in endothelial cells, keratinocytes, normal prostate tissue and prostate tumor tissue, and transformed and hematopoeitic tissue. *See, e.g.,* p. 7, lines 15-16 and p. 35, lines 19-20. Such tissue expression data is not conclusive of the receptor's function or activity as it shows expression in varied tissues types and in both normal and cancerous tissue of the same type;

- As discussed above, the '352 application postulates that various cancerous tissues in mammals express reduced levels of TNFR-6α. However, published data in the scientific literature demonstrates that various types of cancer tissue actually over-express TNFR-6α. *See, e.g., Bai et al.*, PNAS, 97:1230 (2000). It appears that the applicant of the '583 publication recognized this inaccuracy in the '352 application and changed the relevant disclosure in later filings. *See, e.g.,* section [0396] on p. 57 of the '583 publication which the Examiner cited as a basis for the current rejection;

- Numerous statements in the '352 application erroneously suggest that TNFR-6α is a membrane bound receptor. *See, e.g.,* p. 5, lines 4-6; p. 10, lines 27-32; p. 23, lines 18-20; p. 40, lines 2-3; p. 43, lines 5-10. However, TNFR-6α is known to be a soluble decoy receptor. *See, e.g.,* Otsuki et el., Clin. Exp. Immunol., 119:323 (2000);

- The '352 application states that TNFR-6α shares the highest degree of homology to TNFR-1 and TNFR-2, roughly 23%. *See, e.g.,* p. 4, lines 21-23. This is a relatively low percentage of homology between DcR3 and TNFR-1 and-2. DcR3 is a soluble receptor (unlike TNFR-1 and –2 which are membrane-bound receptors) and does not have an intracellular signaling capacity. Accordingly, any inferences, if any, that can be drawn about the activity of TNFR-

6α and TNFR-1 and –2 based on such homology are not a sufficient basis upon which to reasonably predict activity or function; and

- The '352 application states that cells expressing TNFR-6α will have cellular response to TNFR-1 receptor ligands. This is inaccurate for at least two reasons: 1) TNFR-6α does not bind to either of TNFR-1's ligands, namely, TNF-α and lymphotoxin; and 2) TNFR-6α, being a soluble receptor, is not membrane bound like TNFR-1 and does not have an intracellular signaling capacity.

Accordingly, for at least the reasons set forth above, Applicant respectfully requests the Examiner to withdraw the rejection of claims 67-77 and 79-84 under 35 U.S.C. § 102(e) in view of Gentz et al.

Objection to claim 78

The Examiner has objected to claim 78 as being dependent upon rejected claim 77.

In light of Applicant's arguments regarding the '583 publication, Applicant submits that the rejection of claim 77 should be withdrawn, which would obviate the basis of the objection of claim 78.

Information Disclosure Statement

Applicant is submitting herewith a Supplemental Information Disclosure Statement that cites the applications and provisionals referenced by the '583 publication. Applicant requests that Examiner indicate on the record that all such documents have been considered.

In view of the points made above regarding the '583 application, Applicant believes that the application is in condition for allowance and should be passed to issue. If the Examiner is not prepared to pass this application to issue, Applicant respectfully requests that the Examiner or her supervisor contact the undersigned prior to taking any further action in this application.

Respectfully submitted,
GENENTECH, INC.

Date: December 4, 2003 By: _____

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